ORIGINAL

UNITED STATES DISTRICT COURT
FOR THE
DISTRICT OF MASSACHUSETTS

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| **ARIAD PHARMACEUTICALS, INC., MASSACHUSETTS INSTITUTE OF TECHNOLOGY, THE WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH, and THE PRESIDENT AND FELLOWS OF HARVARD COLLEGE**<br><br>**Plaintiffs,**<br>**v.**<br><br>**ELI LILLY AND COMPANY,**<br><br>**Defendant.** | **Civil Action No. 02 CV 11280 RWZ**<br><br>**U.S. District Judge**<br>**Rya W. Zobel** |

**ELI LILLY AND COMPANY'S ANSWER TO PLAINTIFFS' COMPLAINT AND COUNTERCLAIMS**

Defendant, Eli Lilly and Company ("Lilly"), responds to the Complaint of Plaintiffs ARIAD Pharmaceuticals, Inc. ("ARIAD"), Massachusetts Institute of Technology ("M.I.T."), the Whitehead Institute for Biomedical Research ("THE WHITEHEAD INSTITUTE"), and the President and Fellows of Harvard College ("HARVARD") (hereinafter collectively referred to as "Plaintiffs") as follows:

**NATURE OF THE ACTION**

1. This is a patent infringement action against Lilly based on Lilly's activity in connection with its Xigris® and Evista® products covered by claims of Plaintiffs' United States Patent No. 6,410,516 ("the '516 patent"), entitled "Nuclear Factors Associated With Transcriptional Regulation." A copy of the patent is attached as Exhibit 1.

**Answer to Paragraph 1 of the Complaint:**

Lilly admits that Plaintiffs' Complaint alleges claims based on the patent laws. Lilly further admits that a copy of United States Patent No. 6,410,516 ("the '516 patent"), entitled "Nuclear Factors Associated With Transcriptional Regulation" was attached to the Complaint as Exhibit 1. Lilly denies Xigris® and Evista® are covered by any valid claims of the '516 patent. Lilly denies each and every remaining allegation contained in paragraph 1 of the Complaint, and specifically denies that Plaintiffs have any claim against Lilly for patent infringement.

2. Plaintiffs seek monetary damages, including but not limited to a reasonable royalty for Defendant Lilly's current and future infringement of the '516 patent.

**Answer to Paragraph 2 of the Complaint:**

Lilly admits that Plaintiffs' Complaint seeks monetary damages. Lilly denies each and every remaining allegation contained in paragraph 2 of the Complaint.

**PARTIES, JURISDICTION AND VENUE**

3. ARIAD is a corporation organized and existing under the laws of the State of Delaware with its principal place of business located at 26 Landsdowne Street, Cambridge, Massachusetts.

**Answer to Paragraph 3 of the Complaint:**

Lilly is without information sufficient to admit or deny the allegations contained in Paragraph 3 of the Complaint, and therefore denies each and every allegation contained in paragraph 3 of the Complaint.

4. M.I.T is a co-educational, privately endowed research university located at 77 Massachusetts Avenue, Cambridge, Massachusetts.

**Answer to Paragraph 4 of the Complaint:**

Lilly is without information sufficient to admit or deny the allegations contained in Paragraph 4 of the Complaint, and therefore denies each and every allegation contained in paragraph 4 of the Complaint.

5. THE WHITEHEAD INSTITUTE is a non-profit research and education institute located at Nine Cambridge Center, Cambridge, Massachusetts. It is affiliated with M.I.T in its teaching activities, but is wholly responsible for its own research programs, governance, and finance.

**Answer to Paragraph 5 of the Complaint:**

Lilly is without information sufficient to admit or deny the allegations contained in Paragraph 5 of the Complaint and therefore denies each and every allegation contained in paragraph 5 of the Complaint..

6. HARVARD is a co-educational, privately endowed research university located at Massachusetts Hall, Cambridge, Massachusetts.

**Answer to Paragraph 6 of the Complaint:**

Lilly is without information sufficient to admit or deny the allegations contained in Paragraph 6 of the Complaint and therefore denies each and every allegation contained in paragraph 6 of the Complaint..

7. Upon information and belief, Defendant Lilly is a corporation organized and existing under the laws of the State of Indiana with its principal place of business located at Lilly Corporate Center, Indianapolis, Indiana. Lilly does substantial business in this judicial district.

**Answer to Paragraph 7 of the Complaint:**

Lilly admits that it is a corporation organized and existing under the laws of the

State of Indiana with its principal place of business located at Lilly Corporate Center, Indianapolis, Indiana. Lilly admits that it does business in this judicial district. Lilly denies each and every remaining allegation contained in paragraph 7.

8. This is an action for patent infringement under the Patent Act of the United States, 35 U.S.C. § 100 *et seq.*, including §§ 271 and 281. This Court has subject matter jurisdiction over this patent infringement action pursuant to 28 U.S.C. § 1338(a).

**Answer to Paragraph 8 of the Complaint:**

Paragraph 8 of Plaintiffs' Complaint merely purports to describe the nature of the action brought by Plaintiffs. To the extent an answer is required, Lilly admits that Plaintiffs base their claims on the patent laws of the United States 35 U.S.C. § 100 *et seq.*, including §§ 271 and 281. Except as so admitted, Lilly denies each and every remaining allegation contained in paragraph 8 of the Complaint, and specifically denies that Plaintiffs have any claim against Lilly for patent infringement. Lilly does not contest the Court's subject matter jurisdiction pursuant to 28 U.S.C. § 1338(a).

9. Venue is proper in this judicial district pursuant to §§ 1400(b) and 1391(c).

**Answer to Paragraph 9 of the Complaint:**

Lilly does not contest that venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1400(b) and 1391(c).

**FACTUAL BACKGROUND**

10. Living cells respond to a vast array of different signals in their environment, including natural regulatory factors (e.g. hormones) and harmful factors (e.g.

toxins). A primary way that cells respond to such signals is through intricate networks of signaling proteins inside the cell, which act as "messengers" to regulate expression of genes that are critical for normal cell function. Normal cell signaling and gene regulation are both controlled at a molecular level by specific interactions of these "messenger" proteins with other proteins and DNA. Identifying these "messenger" proteins and how they function is a crucial step in developing drugs for treating diseases associated with abnormal cell signaling and gene regulation.

**Answer to Paragraph 10 of the Complaint:**

Lilly admits that living cells respond to a vast array of different signals in their environment. Except as so admitted, Lilly cannot admit or deny the remaining allegations contained in paragraph 10 of the Complaint to the extent paragraph 10 does not contain allegations of fact. To the extent paragraph 10 of the Complaint does contain additional allegations of fact, Lilly denies each and every such allegation.

11. The invention of the '516 patent arose from a collaboration between research groups at three of the world's leading biomedical research institutions, M.I.T., THE WHITEHEAD INSTITUTE, and HARVARD. The collaboration was directed by three distinguished scientists, Dr. David Baltimore, Nobel Laureate and former director of THE WHITEHEAD INSTITUTE, Dr. Phillip Sharp, also a Nobel Laureate and now Institute Professor at M.I.T., and Dr. Thomas Maniatis, Thomas H. Lee Professor of Molecular and Cellular Biology at HARVARD.

**Answer to Paragraph 11 of the Complaint:**

Lilly is without knowledge or information sufficient to form a belief as to the truth of the allegations contained in paragraph 11 of the Complaint and therefore denies each and every allegation contained in paragraph 11 of the Complaint.

12. In the mid 1980s, Dr. Baltimore and his colleagues identified a "messenger" protein, which they named "NF-KB." As discussed in the '516 patent specification, Dr. Baltimore and his colleagues initially believed that NF-KB was

only found in certain cells known as "B cells" and therefore, had a limited role in cell signaling and gene regulation.

**Answer to Paragraph 12 of the Complaint:**

Lilly is without knowledge or information sufficient to form a belief as to the truth of the allegations contained in paragraph 12 of the Complaint and therefore denies each and every allegation contained in paragraph 12 of the Complaint.

13. Extensive studies on NF-KB carried out by the named inventors in Dr. Baltimore's laboratory at THE WHITEHEAD INSTITUTE and the other co-inventors in Dr. Sharp's laboratory at M.I.T. and Dr. Maniatis' laboratory at HARVARD led to the surprising discovery, described in the '516 patent, that NF-KB is found in "many, if not all, cell types and that it acts as an intracellular messenger capable of playing a broad role in gene regulation as a mediator of inducible signal transduction." ('516 patent col. 2, lines 29-31.) Most significantly, through the work disclosed in the '516 patent, the inventors also showed how the NF-KB cell-signaling pathway could be regulated and used for medical and therapeutic applications.

**Answer to Paragraph 13 of the Complaint:**

Lilly is without knowledge or information sufficient to form a belief as to the truth of the allegations contained in paragraph 13 of the Complaint and therefore denies each and every allegation contained in paragraph 13 of the Complaint.

14. ARIAD, since its founding in 1991, has been engaged in research and development of pharmaceutical products that regulate cell signaling pathways and gene function. ARIAD's drug discovery program is aimed at developing small-molecule drugs to inhibit or block disease-related abnormal cell-signaling and to control gene function and cell-signaling.

**Answer to Paragraph 14 of the Complaint:**

Lilly is without knowledge or information sufficient to form a belief as to the truth of the allegations contained in paragraph 14 of the Complaint and therefore denies each and every allegation contained in paragraph 14 of the Complaint.

15. In part for his preeminent contribution to the cell-signaling field and the relevance of this expertise to ARIAD's research and development program, ARIAD invited, and Dr. Baltimore agreed, to join ARIAD's board of scientific and medical advisors as a founding member.

**Answer to Paragraph 15 of the Complaint:**

Lilly is without knowledge or information sufficient to form a belief as to the truth of the allegations contained in paragraph 15 of the Complaint and therefore denies each and every allegation contained in paragraph 15 of the Complaint.

16. In 1986, the first of a series of U.S. patent applications relating to the NF-KB research spearheaded by Dr. Baltimore and various of his co-inventors was filed. Through extensive prosecution, during which the Patent Office carefully scrutinized the claimed subject matter for compliance with the statutory requirements for patentability, the Patent Office awarded the inventors several patents claiming various, separate aspects of this pioneering technology. The '516 patent asserted herein, is the most recent patent to issue of this family of patents.

**Answer to Paragraph 16 of the Complaint:**

Lilly admits that the '516 patent claims priority as a continuation-in-part of United States Patent Application Serial Number 06/871,441 filed January 9, 1986. Lilly denies each and every remaining allegation contained in paragraph 16 of the Complaint.

**THE PATENT-IN-SUIT**

17. On June 25, 2002, the '516 patent, entitled "Nuclear Factors Associated With Transcriptional Regulation," with claims that cover methods of treating human disease by regulating NF-KB activity, was duly and legally issued to Baltimore *et al.* and assigned to M.I.T., THE WHITEHEAD INSTITUTE, and HARVARD.

**Answer to Paragraph 17 of the Complaint:**

Lilly admits United States Patent No. 6,410,516 ("the 516 patent") states on its face that it issued on June 25, 2002. Lilly admits that the inventors named on the face of United States Patent No. 6,410,516 are Baltimore *et al.* Lilly admits that the Assignees named on the face of United States Patent No. 6,410,516 are M.I.T., THE WHITEHEAD INSTITUTE, and HARVARD, but Lilly is without knowledge or information sufficient to form a belief as to whether or when the '516 patent was assigned to M.I.T., THE WHITEHEAD INSTITUTE, and HARVARD and therefore denies such allegation. Otherwise, Lilly denies each and every remaining allegation contained in paragraph 17 of the Complaint.

18. Based on a license agreement executed in 1991, ARIAD is the exclusive licensee from M.I.T., THE WHITEHEAD INSTITUTE, and HARVARD of the '516 patent, which presents claims directed to one aspect of the pioneering technology discovered by the inventors, i.e., the use of drugs that regulate NF-KB cell signaling.

**Answer to Paragraph 18 of the Complaint:**

Lilly is without knowledge or information sufficient to form a belief as to the existence of a license agreement between ARIAD, M.I.T., THE WHITEHEAD INSTITUTE and HARVARD, or whether such an agreement was executed in 1991, and therefore denies such allegation. Lilly denies each and every remaining allegation contained in paragraph 18 of the Complaint.

**LILLY'S INFRINGEMENT OF THE '516 PATENT**

19. Upon information and belief, Lilly is engaged in the manufacture, importation, use, sale and/or offers of sale, and promotion of pharmaceutical products marketed under the brandname Evista®.

**Answer to Paragraph 19 of the Complaint:**

Lilly admits that it is engaged in the manufacture, use, sale and/or offers of sale, and promotion of raloxifene hydrocholoride marketed under the brandname Evista®. Except as so admitted, Lilly denies each and every remaining allegation.

20. Upon information and belief, Evista® is a form of the selective estrogen receptor modulator raloxifene hydrocholoride, and was approved for sale by the United States Food and Drug Administration on or about December 10, 1997, for the prevention and treatment of osteoporosis in postmenopausal women.

**Answer to Paragraph 20 of the Complaint:**

Lilly admits that Evista® is a form of the selective estrogen receptor modulator raloxifene hydrocholoride, and was approved for sale by the United States Food and Drug Administration in December 1997 for the prevention and treatment of osteoporosis in postmenopausal women. Except as so admitted, Lilly denies each and every remaining allegation.

21. Upon information and belief, a molecular basis for the action of Evista® in treating osteoporosis has been demonstrated to occur through the modulation of NF-KB activity. Some of these findings were published by Lilly scientists in a World Intellectual Property Organization Patent Application entitled "Methods of Modulating NF-KB Transcription Factor" and bearing publication number WO 96/40137. A copy of this patent application is attached as Exhibit 2.

**Answer to Paragraph 21 of the Complaint:**

Lilly admits that Lilly scientists are named as inventors on the World Intellectual Property Organization Patent Application entitled "Methods of Modulating NF-KB Transcription Factor." Lilly admits that the patent application bears publication number WO 96/40137. Lilly admits that World Intellectual Property Organization Patent Application entitled "Methods of Modulating NF-KB Transcription Factor" claimed

methods of modulating NF-KB transcription factor comprising administering to a human in need of an effective amount of a certain compound. Lilly further admits that a copy of the World Intellectual Property Organization Patent Application entitled "Methods of Modulating NF-KB Transcription Factor" and bearing publication number WO 96/40137 was attached to the Complaint as Exhibit 2. Lilly denies each and every remaining allegation in paragraph 21 of the Complaint. Except as so admitted, Lilly denies each and every remaining allegation.

> 22. Upon information and belief Lilly is engaged in the manufacture, importation, use, sale and/or offers of sale and promotion of pharmaceutical products marketed under the brandname Xigris®.

**Answer to Paragraph 22 of the Complaint:**

Lilly admits that it is engaged in the manufacture, use, sale and/or offers of sale, and promotion of a form of recombinant human activated protein C marketed under the brandname Xigris®. Except as so admitted, Lilly denies each and every remaining allegation.

> 23. Upon information and belief, Xigris® is a form of recombinant human activated protein C, and was approved for sale by the United States Food and Drug Administration on or about November 21, 2001, for the reduction of mortality in human adult patients with severe sepsis who have a high risk of death.

**Answer to Paragraph 23 of the Complaint:**

Lilly admits that Xigris® is a form of recombinant human activated protein C, and was approved for sale by the United States Food and Drug Administration on or about November 21, 2001 for the reduction of mortality in human adult patients with severe sepsis who have a high risk of death. Except as so admitted, Lilly denies each and

every remaining allegation.

24. Upon information and belief, a molecular basis for the action of Xigris® in treating septic shock has been demonstrated to occur through the inhibition of NF-KB activity. These findings were published by Lilly scientists in papers by Joyce *et al.*, J. Biol. Chem., 276: 11199-11203, 2001 and Crit. Care Med. 30:S288-S293, 2002. Copies of these papers are attached as Exhibits 3 and 4.

**Answer to Paragraph 24 of the Complaint:**

Lilly admits that Lilly scientists published papers in J. Biol. Chem., 276: 11199-11203, 2001 and Crit. Care Med. 30:S288-S293, 2002. Lilly admits that copies of Joyce *et al.*, J. Biol. Chem., 276: 11199-11203, 2001 and Crit. Care Med. 30:S288-S293, 2002 were attached to the Complaint as Exhibits 3 and 4 respectively. Lilly denies each and every remaining allegation in paragraph 24 of the Complaint.

25. Plaintiffs have suffered and will continue to suffer damages as a result of Lilly's infringing activities.

**Answer to Paragraph 25 of the Complaint:**

Lilly denies each and every allegation contained in paragraph 25 of the Complaint.

26. Plaintiffs have previously sought to initiate discussions with Lilly concerning a license to Plaintiffs' NF-KB patent estate. Defendant Lilly has failed to respond to these efforts.

**Answer to Paragraph 26 of the Complaint:**

Lilly admits that one or more of Plaintiffs contacted Lilly with respect to other patents in their portfolio. Lilly denies that Plaintiffs have sought to initiate discussions with Lilly concerning the '516 patent-in-suit. Lilly denies each and every remaining allegation in paragraph 26 of the Complaint.

## COUNTS

### Count 1 – Patent Infringement of the '561 Patent

27. Paragraphs 1-26 of this Complaint are incorporated by reference as if stated fully herein.

**Answer to Paragraph 27 of the Complaint:**

Lilly incorporates herein by reference its responses to paragraphs 1-26 of the Complaint.

28. Defendant Lilly, by engaging in the unauthorized manufacture, importation, use, sale and/or offers for sale of raloxifene hydrochloride in the United States, including pharmaceutical products marked as Evista®, has committed acts of direct, contributory and/or induced infringement of claims 69-72, 80, 82, 84, 85 and 93-96 of the '516 patent.

**Answer to Paragraph 28 of the Complaint:**

Lilly denies each and every allegation contained in paragraph 28 of the Complaint.

29. Defendant Lilly, by engaging in the unauthorized manufacture, importation, use, sale and/or offers for sale of recombinant human activated protein C in the United States, including pharmaceutical products marketed as Xigris®, has committed acts of direct, contributory and/or induced infringement of claims 14, 15, 144-146, and 154-156 of the '516 patent.

**Answer to Paragraph 29 of the Complaint:**

Lilly denies each and every allegation contained in paragraph 29 of the Complaint.

30. Defendant Lilly has offered for sale, sold and/or imported raloxifene hydrochloride into the United States, including pharmaceutical products marketed as Evista®, with knowledge that such products have a molecular basis of action through the modulation of NF-KB activity and are especially made or adapted for

use in an infringment of the '516 patent. Evista®, which constitutes a material part of the invention, is not a staple article or commodity of commerce suitable for substantial non-infringing use. By its actions, Defendant Lilly is actively and knowingly inducing infringement of claims 69-72, 80, 82, 84, 85 and 93-96 of the '516 patent.

**Answer to Paragraph 30 of the Complaint:**

Lilly admits that it has offered for sale, sold and/or imported raloxifene hydrochloride into the United States, including pharmaceutical products marketed as Evista®. Lilly denies each and every remaining allegation contained in paragraph 30 of the Complaint.

31. Defendant Lilly has offered for sale, sold and/or imported recombinant human activated protein C into the United States, including pharmaceutical products marketed as Xigris®, with knowledge that such products have a molecular basis of action through the inhibition of NF-KB activity and are especially made or adapted for use in an infringement of the '516 patent. Xigris® which constitutes a material part of the invention, is not a staple article or commodity of commerce suitable for substantial non-infringing use. By its actions, Defendant Lilly is actively and knowingly inducing infringement of claims 14, 15, 144-146, and 154-156 of the '516 patent.

**Answer to Paragraph 31 of the Complaint:**

Lilly admits that it has offered for sale, sold and/or imported recombinant human activated protein C into the United States, including pharmaceutical products marketed as Xigris®. Lilly denies each and every remaining allegation contained in paragraph 31 of the Complaint.

32. Plaintiffs have suffered and will continue to suffer damages as a result of Defendant's infringing activities.

**Answer to Paragraph 32 of the Complaint:**

Lilly denies each and every allegation contained in paragraph 32 of the Complaint. Lilly specifically denies that the Plaintiffs are entitled to their requested relief.

## AFFIRMATIVE AND OTHER DEFENSES

### FIRST AFFIRMATIVE DEFENSE

### Non-infringement

34. Lilly does not infringe any valid claim of United States Patent No. 6,410,516.

### SECOND AFFIRMATIVE DEFENSE

### Patent Invalidity

35. The claims of United States Patent No. 6,410,516 are invalid for failing to meet the requirements of one or more of the provisions of 35 U.S.C §§ 101, 102, 103 and/or 112.

36. U.S. Patent No. 6,410,516 is invalid for the prosecution form of laches.

### THIRD AFFIRMATIVE DEFENSE

### Patent unenforceability for Inequitable Conduct

37. United States Patent No. 6,410,516 is unenforceable as the result of the inequitable conduct during the prosecution of the application that issued as the '516 patent. The Plaintiffs and/or their representatives committed inequitable acts that misled the Patent and Trademark Office. In particular, persons associated with the filing and prosecution of the application on Plaintiffs' behalf, having knowledge of the United States Patent No. 4,418,068 ("the Jones Patent"), willfully or with gross negligence failed to disclose the Jones patent to the Patent and Trademark Office during prosecution and, therefore violated their duty of disclosure under 37 CFR 1.56.

38. Plaintiffs, through their attorneys, filed this action on June 25, 2002, the very day that the '516 patent in suit issued. The persons associated with the filing and prosecution of the application that matured as the '516 patent were, on information and belief, aware of the complaint in this action and the references cited therein prior to June 25, 2002, and thus prior to the issuance of the '516 patent. Plaintiffs and their attorneys attached to the complaint in this action as "Exhibit 2" a World Intellectual Property Organization Patent Application 96/40137 entitled "Methods of Modulating NF-KB Transcription Factor." ("WO application"). The Jones Patent, which discloses the administration of raloxifene hydrochloride before the priority dates for the '516 patent, was incorporated by reference in that application. (See p. 4 lines 10-14 of the WO application). Thus, the persons associated with the filing and prosecution of the application that issued as the '516 patent, including Plaintiffs and their attorneys, knew or should have known of the prior art Jones patent before the issuance of the '516 patent, yet failed to disclose it to the U.S. Patent and Trademark Office.

39. The Jones Patent discloses the use of raloxifene hydrochloride as "pharmaceuticals for antiestrogen and antiandrogen therapy" in the treatment of mammary and prostatic tumors. This prior art reference specifically describes administering "an effective dose of a compound as described to a subject suffering from such a condition or at risk of suffering from such condition." (Jones Patent, col. 1, lines 33-37). The Jones Patent describes giving such formulations to mammals (cols. 28 et seq.) and teaches administration to humans of up 1000 mg/day of raloxifene hydrochloride (col. 38 et seq.), well in excess of the preferred range taught by the WO application.

40. Plaintiffs and their counsel attached the WO application as evidence that the administration of raloxifene hydrochloride, as taught in the prior art Jones Patent, "modulat[es] NF-κB activity." Complaint, ¶ 21. The WO application itself states that raloxifene hydrochloride is "effective in blocking the action of the important cellular regulatory molecule NF-κB." (WO application, p. 12). As such, the Jones Patent is clearly material prior art that anticipates one or more of the claims of the '516 patent.

41. Moreover, on information and belief, plaintiffs, one or more of the inventors, and/or their attorneys were clearly aware of a variety of articles that teach that the inhibition of NF-κB is an inherent property of a number of compounds that were commonly administered in the prior art. Indeed, the inherency of NF-κB modulation in many of these prior art compounds was described by one of the co-inventors in a review article published while the application was still pending, Baldwin AS Jr., *Series Introduction: the transcription factor NF-kB and human disease*, J. Clin. Invest., Jan; 107(1):3-6 (2001). *See also* E. Kopp and S. Ghosh, *Inhibition of NF-κB by Sodium Salicylate and Aspirin,* SCIENCE 265: 956-959 (1994) (Aspirin), Yumi Yamamoto, et al., *Sulindac Inhibits Activation of the NF-κB Pathway*, 274 J. BIOL. CHEM. 27307 (1999) (Sulindac and its metabolites); Albert S. Baldwin, Jr., *The NF-κB and IκB Proteins: New Discoveries and Insights*, 14 ANN. REV. IMMUNOL. 649, 671 (1996) (Prednisone and other Glucocorticoids); N. Auphan, J. DiDonato, C. Rosette, A. Helmberg and M. Karin, Immunosuppression by Glucocorticoids: Inhibition of NF-κB Activity Through Induction of IκB Synthesis, Science, Vol. 270:286-290 (1995) (same); Albert S. Baldwin, Jr., *The NF-κB and IκB Proteins: New Discoveries and Insights*, 14 ANN. REV. IMMUNOL. 649, 671 (1996) (Cyclosporin A); Kye-Im Jeon, Jae-Yeon Jeong and Dae-Myung Jue, *Thiol-*

*reactive Metal Compounds Inhibit NF-κB Activation By Blocking IκB kinase*, J. Immunol. 164 (11): 5981-5989 (June 1, 2000) (Gold Compounds); Luis Miguel Blanco-Colio, et al., *Red Wine Intake Prevents Nuclear Factor-κB Activation in Peripheral Blood Mononuclear Cells of Healthy Volunteers During Postprandial Lipemia*, CIRCULATION, 102: 1020 (2000) (Red Wine); Fajun Yang, et al., Green Tea Polyphenols Block Endotoxin-Induced TNF-Production and Lethality in a Murine Model, 128 J. Nutr. 2334 (1998) (Green Tea); Suppression of Lipopolysaccharide-Induced Nuclear Factor-κB Activity by Theaflavin-3,3'-Digallate from Black Tea and Other Polyphenols through Downregulation of IκB Kinase Activity in Macrophages, 59 Biochem. Phamacol. 357 (2000) (Black Tea); M.M. Manson, et al., *Modulation of signal-transduction pathways by chemopreventive agents*, 28 BIOCHEM. SOC. TRANS. 7 (2000) (Turmeric); and Nagaotshi Ide and Benjamin H.S. Lau, Garlic Compounds Minimize Intracellular Oxidative Stress and Inhibit Nuclear Factor-κB Activation, 131 J. Nutr. 1020S (2001) (Garlic). None of these references, though clearly material to the prosecution of the application that issued as the '516 patent, were disclosed to the examiner.

42. Thus, persons associated with the filing and prosecution of the application that led to the '516 patent, including Plaintiffs, the inventors, and their attorneys, were clearly aware of the Jones Patent and/or other prior art references and their high materiality to the patent application examination process during the pendency of the prosecution of that application. This material information is not cumulative, and thus should have been disclosed. Therefore, the '516 patent is unenforceable as the result of inequitable conduct.

## COUNTERCLAIMS FOR DECLARATORY RELIEF

43. Defendant and counterclaimant, Lilly asserts this counterclaim against Plaintiffs and Counterdefendants ARIAD, M.I.T, THE WHITEHEAD INSTITUTE, and HARVARD and avers as follows:

## JURISDICTION AND VENUE

44. This action arises under the patent laws of the United States, 35 U.S.C. §§ 1 et seq. This Court has original jurisdiction under 28 U.S.C. §§1331, 1338(a) and Fed. R. Civ. P. 13(a). Counterclaimant Lilly seeks declaratory judgment pursuant to Sections 2201 and 2202 of Title 28 of the United States Code.

45. There is an actual controversy within this judicial district arising under the patent laws of the United States, 35 U.S.C. § 1 *et seq.*, and Declaratory Judgments Act, 28 U.S.C. §§ 2201 *et seq.*, between Counterclaimant and Counterdefendants. Plaintiffs initiated this action against Lilly, alleging infringement by Lilly of United States Patent No. 6,410,516. An actual controversy exists at least by virtue of Plaintiffs' Complaint and Lilly's Answer thereto, asserting non-infringement, and invalidity of the patent in suit.

46. Venue for these Counterclaims is proper under 28 U.S.C. § 1391 (b) and (c) and 1400 (b).

**PARTIES**

47. Upon information and belief based upon representations made in Plaintiff's Complaint, ARIAD is a corporation organized and existing under the laws of the State of Delaware with its principal place of business located at 26 Landsdowne Street, Cambridge, Massachusetts.

48. Upon information and belief based upon representations made in Plaintiff's Complaint, M.I.T is a co-educational, privately endowed research university located at 77 Massachusetts Avenue, Cambridge, Massachusetts.

49. Upon information and belief based upon representations made in Plaintiff's Complaint, THE WHITEHEAD INSTITUTE is a non-profit research and education institute located at Nine Cambridge Center, Cambridge, Massachusetts.

50. Upon information and belief based upon representations made in Plaintiff's Complaint, HARVARD is a co-educational, privately endowed research university located at Massachusetts Hall, Cambridge, Massachusetts.

51. Defendant Lilly is a corporation organized and existing under the laws of the State of Indiana with its principal place of business located at Lilly Corporate Center, Indianapolis, Indiana.

52. U.S. Patent No. 6,410,516, which issued June 25, 2002, references on its face a priority date of January 9, 1986, more than sixteen years prior.

53. Plaintiffs have charged Lilly with infringement of United States Patent No. 6,410,516, for the sale of products whose active ingredients were taught for administration in humans in patent applications filed before the earliest claimed priority date of the '516 patent.

54. Plaintiffs did not seek to add the claims asserted against Lilly's accused products to the patent application that issued as the '516 patent until after Lilly had commercialized its accused products.

**COUNTERCLAIM I – NON-INFRINGEMENT AND INVALIDITY**

55. Lilly has not infringed any valid claim of United States Patent No. 6,410,516 in any way, i.e., directly, contributorily, or by inducement. Therefore, Lilly is entitled to a judicial declaration that Lilly has not and does not infringe United States Patent No. 6,410,516.

56. United States Patent No. 6,410,516 is invalid for failure to comply with one or more of the requirements, conditions and provisions set forth in at least 35 U.S.C. §§ 101, 102, 103, and/or 112. Therefore, Lilly is entitled to a judicial declaration that the United States Patent No. 6,410,516 is invalid and unenforceable.

57. United States Patent No. 6,410,516 is invalid for the prosecution form of laches.

**COUNTERCLAIM II - UNENFORCEABILITY**

58. Lilly incorporates by reference the fact and allegations set forth in Paragraphs 37-42, supra.

59. United States Patent No. 6,410,516 is unenforceable due to inequitable conduct. Therefore, Lilly is entitled to a judicial declaration that the United States Patent No. 6,410,516 is unenforceable.

## RELIEF REQUESTED

WHEREFORE, defendant-counterclaimant Lilly prays for judgment and relief against Plaintiff-counterdefendants, ARIAD, M.I.T, THE WHITEHEAD INSTITUTE, and HARVARD including:

(A) A dismissal with prejudice of Plaintiffs' Complaint and a denial of plaintiffs' claims for relief against defendant-counterclaimant Lilly.

(B) A declaration that defendant-counterclaimant has not infringed any valid claim of United States Patent No. 6,410,516.

(C) A declaration that United States Patent No. 6,410,516 is invalid.

(D) A declaration that United States Patent No. 6,410,516 is unenforceable.

(E) An injunction permanently preventing counterdefendants from asserting or enforcing United States Patent No. 6,410,516 against Lilly and/or purchasers or users of Lilly products.

(F) Judgment that this is an exceptional case and that defendant-counterclaimant be awarded costs, expenses and reasonable attorney's fees pursuant to 35 U.S.C. §285.

(G) Awarding such other and further relief as this Court may deem just and proper.

May 27, 2003

Respectfully submitted,

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**CERTIFICATE OF SERVICE**

I, Jenny E. Macioge, hereby certify that on May 27, 2003, a true and correct copy of the foregoing was served by the indicated means to the persons at the addresses listed:

ELI LILLY and COMPANY'S ANSWER TO PLAINTIFFS' COMPLAINT AND COUNTERCLAIMS

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Kerry L. Timbers
Anne Marie Longobucco
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☐ Via Hand Delivery
☐ Via Overnight Courier
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